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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/994,937	11/28/2001	David M. Anderson	05900002AA	7327

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EXAMINER	
FISHER, ABIGAIL L	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/994,937	ANDERSON, DAVID M.	
	Examiner	Art Unit	
	ABIGAIL FISHER	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-27,29-53,56,58-60 and 65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-19,27,29-44,52,53,56,58-60 and 65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of Amendments/Remarks filed and Declaration under 37 CFR 1.132 on October 14 2008 is acknowledged. Claims 2, 28, 54-55, 57 and 61-64 were/stand cancelled. Claim 65 was added. Claims 1, 3-27, 29-53, 56, 58-60 and 65 are pending. Claims 20-26 and 45-51 are withdrawn as being directed to a non-elected invention. Claims 1, 3-19, 27, 29-44, 52-53, 56, 58-60 and 65 are directed to the elected invention.

The examiner notes the previous election of paclitaxel as the active, water as the polar solvent, spearmint oil as the essential oil, gentisic acid as the dissolution/solublization agent, and pluronics as the surfactant.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 3-19, 27, 29-44, 52-53, 56, 58-60 and 65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Landh et al. (US Patent No. 5531925, cited in the Office action mailed on 4/14/08) in view of Benet et al. (US Patent No. 5716928, cited in the Office action mailed on April 6 2006) and Yau et al. (US Patent No. 5541287, cited in the Office action mailed on 4/14/08) as evidenced by The Merck Index (2006, cited in the Office action mailed on 4/14/08).

Applicant Claims

Applicant claims a composition comprising a structured fluid selected from the group consisting of a reversed cubic liquid phase and a reversed hexagonal liquid crystalline phase, and a combination thereof comprising a polar solvent, a surfactant, and a essential oil or a dissolution/solublization agent or both; and a compound that is present in an effective amount in said structured fluid.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Landh et al. is directed to particles, especially colloidal particles, made from reversed cubic, hexagonal or intermediate phases, or L3 phases, or mixtures thereof (column 7, Lines 51-54). The invention of Landh et al. is in the field of lipid-based dispersed vehicles representing novel drug delivery systems (column 7, Lines 61-62). The particles according to the invention comprise an interior phase of a non-lamellar lyotropic liquid crystalline phase selected from the group consisting of a reversed cubic liquid crystalline phase, a reversed intermediate liquid crystalline phase and a reversed hexagonal liquid crystalline phase, or a homogeneous L3 phase, or any combination thereof, and surface phase selected from the group consisting of a lamellar crystalline

phase and a lamellar liquid crystalline phase, or an L3 phase, or any combination thereof (column 8, Lines 27-36). The phases are prepared by a novel fragmentation. The fragmentation procedure guarantees the coexistence of the phase making up the interior, the phase making up the surface, and the solvent-rich solution phase. The solvent rich solution phase is rich in water or any other polar solvent (column 8, lines 41-56). Reversed cubic liquid crystalline phase can be generally fragment by the incorporation of fragmentation agents belonging to the group of block copolymers with a hydrophilic lipophilic balance greater than 15, examples include poloxamers (column 10, liens 30-44). Landh et al. teach that the invention is well suited to the formulation and delivery of hydrophobic compounds that have limited aqueous solubility (column 20, lines 3-6). The invention is not restricted to any particular route of administration. Administration can be made by intravenous, intramuscular, intranasal, ocular, sublingual, subcutaneous, oral, rectal, vaginal, or dermal routes, or regionally such as through intraperitoneal, intraarterial, intrathecal and intravesical routes (column 20, Lines 48-53).

Landh et al. also teach the particles being in a pharmaceutical composition consisting of the particles and a pharmaceutically acceptable carrier.
(See column 32, Claim 19).

Landh et al. teach the invention's applicability in the field of cancer therapy. The invention of Landh et al. provides prolonged circulation as compared to the free drug, protection and stabilization of the drug, circumvention of certain cell membrane barriers, and amplification of the drug effect due to targeted drug deliver. Specific cancer

therapeutics include taxol (column 25, section 4.1.6). As evidenced by The Merck Index, Taxol is one of the brand names of paclitaxel.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Landh et al. does not specify the incorporation of an essential oil. However, this deficiency is cured by Benet et al.

Benet et al. is directed to the use of essential oils to increase the bioavailability of oral pharmaceutical compounds. It is disclosed that essential oils were found to increase drug bioavailability by inhibiting drug biotransformation (column 2, lines 52-54). Essential oils listed as suitable include clove bud and spearmint (table 1). The essential oils are coadministered with the drug to provide the increased drug bioavailability. Coadministration can occur with the same delivery vehicle or with different delivery vehicles (column 25, 27-28). Pharmaceutical compounds listed as having their bioavailability increased with coadministration of an essential oil include steroids and taxol (claim 5).

Landh et al. does not specify the incorporation of gentisic acid. However, this deficiency is cured by Yau et al.

Yau et al. is directed to methods, compounds, compositions and kits to pretargeted delivery of diagnostic and therapeutic agents. Gentisic acid is disclosed as an effective radioprotectant (example 18).

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been obvious to one of ordinary skill in the art to combine the teachings of Landh et al. and Benet et al. and utilize essential oils such as spearmint in the invention of Landh et al. One of ordinary skill in the art would have been motivated to incorporate essential oils into the invention of Landh et al. because Benet et al. indicate that essential oils increase the bioavailability of oral pharmaceutical compounds when coadministered. Additionally, as taught by Benet et al. the essential oils can be coadministered with the same delivery vehicle of the drug. Pharmaceutical compounds listed by Benet et al. as having increased drug bioavailability is taxol. Since Landh et al. is also directed at delivering cancer therapeutics, one of ordinary skill in the art would expect that the incorporation of essential oils would have at least an additive effect in terms of drug delivery.

It would have been obvious to one of ordinary skill in the art to combine the teachings of Landh et al. and Yau et al. and utilize gentisic acid in the composition. One of ordinary skill in the art would have been motivated to utilize gentisic acid because it is taught by Yau et al. as being a radioprotectant. Therefore, when utilizing the invention of Landh et al. for cancer treatment, which besides chemotherapy includes radiology, it would have been obvious to one of ordinary skill in the art to include gentisic acid which is a known radioprotectant.

It would have been obvious to one of ordinary skill in the art to combine the teachings of Landh et al., Benet et al., and Yau et al. and utilize both essential oils and gentisic acid in the composition of Landh et al. One of ordinary skill in the art would have been motivated to include these agents because Landh et al. is directed to

delivering cancer therapeutics and Benet et al. teaches that essential oils increase the bioavailability of taxol and Yau et al. teaches that gentisic acid is a radioprotectant. Therefore, one of ordinary skill in the art would expect that the incorporation of these components in the composition of Landh et al. would have at least an additive effect in cancer therapy.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Regarding the functional imitations of claims 5-9, 12-13, 27, 31-34, 37-39, and 53, Benet teaches the elected species of essential oil, spearmint oil, and Yau teaches the elected species of dissolution/solublization agent. Therefore, these species necessarily posses the functional limitations of the instant claims.

Response to Arguments and Rule 132 Declaration

Applicants argue that (1) without the fourth component either the cubic phase would not form at all or it would form but with only significantly lower levels of incorporation of the drug. The declaration of Anderson shows different formulations either with or with the essential oil and shows that when 3 mg/mL paclitaxel was added into the cubic phase of Landh, the paclitaxel precipitated out. Applicant argues that (2) poloxamers are identified in both Landh and the instant invention however the poloxamers taught by Landh have a higher HLB than that of the instant invention.

Applicant argues that water insoluble poloxamers (low HLB) are called for. The declaration by Anderson also reiterates this point. Applicant argues that (3) the teachings of Landh do not identify the problem of drugs with no or limited loading and contains no mention of spacing in the bilayer or polar identify of a drug. Applicant argues that (4) Gentisic acid is neither shown or suggested as relevant to the solubilization of paclitaxel. Applicant argues that (5) the incorporation of essential oils into the invention of Landh tends to destroy the cubic phase materials. The declaration of Anderson shows that incorporation of essential oils into the cubic phase of Landh was found to be destructive. Applicant argues that the examples in Landh are not capable of taking up significant levels of essential oils. Applicant argues that (6) Benet teaches co-administration of essential oils to increase bioavailability does not suggest the direct incorporation of essential oils into complex structured fluid formulation.

Applicants' arguments filed October 14 2008 have been fully considered but they are not persuasive. The declaration under 37 CFR 1.132 filed October 14 2008 is insufficient to overcome the rejection of the claims.

Regarding applicant's first and third arguments, the instant claims as currently written only require an effective amount of a compound that is otherwise les than 5% (by weight soluble in soybean oil). Therefore is no requirement that this "effective amount" can not be significantly low. As the examiner understands, one feature of the instant invention is incorporation of higher amounts of an active agent. However, this instant claims only require an "effective amount". This can be very low for example 0.5mg//ml and still be considered an "effective amount. Therefore, applicant's

arguments are directed to features that are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Regarding applicants second argument, the instant claims only recite a lipid or a surfactant. Therefore, any surfactant can be included. Furthermore, the specific poloxamer taught by Landh et al. is poloxamer 188. The instant specification specifically lists poloxamer 188 as a preferred surfactant (page 50, lines 21-22). Therefore, this argument is not persuasive.

Regarding applicant's fourth argument, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Since the instant invention is directed to a product and it would have been obvious to one of ordinary skill in the art to add gentisic acid, the fact that applicant utilizes it to solubilize paclitaxel does not patentably distinguish it from the prior art.

Regarding applicant's fifth argument, the instant claims do not require a particular amount of essential oil is added. Benet teaches that percentages of essential oils utilized are 1, 2 and at least 5%. The examples in the declaration utilize 10% of an essential oil. Therefore, the arguments and declaration are not persuasive because one of ordinary skill in the art after looking at the teachings of Benet would have been motivated to add 1, 2 or 5% of an essential oil and the evidence presented does not

show that that these lower amounts of essential oil are destructive to the Landh invention. Although, applicant argues that Landh is not capable of taking up significant levels of essential oils, the instant claims do not require a significant level of essential oil. Therefore, applicant is arguing features which are not in the instant claims.

Regarding applicant's sixth argument, Landh clearly teach the incorporation of hydrophobic drugs such as taxol. Benet teaches that the addition of essential oils increases the bioavailability of hydrophobic pharmaceutical compounds and specifically teaches that one of those compounds is taxol. Therefore, one of ordinary skill in the art would have been motivated to add an essential oil to increase the bioavailability in the invention of Landh which is a drug delivery vehicle.

Therefore, the rejection is maintained since applicant has not provided any persuasive arguments to overcome the rejection.

Double Patenting/Terminal Disclaimer

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory

double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The rejection of claims 1, 3-19, 27, 29-44, 52-53, 56 and 58-60 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-7, 9-15, 17-36, 38-39 and 74-75 of copending Application 10/460659 in view of Yau et al. is **withdrawn** in light of the filing of a Terminal Disclaimer on October 14 2008.

The rejection of claims 1, 3-19, 27, 29-44, 52-53, 56 and 58-60 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-84 of U.S. Patent No. 6991809 is **withdrawn** in light of the filing of a Terminal Disclaimer on October 14 2008.

The terminal disclaimers filed on October 14 2008 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US Patent No. 6991809 and any patent granted on Application No. 10460659 have been reviewed and are accepted. The terminal disclaimers have been recorded.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ABIGAIL FISHER whose telephone number is (571)270-3502. The examiner can normally be reached on M-Th 9am-6pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Examiner
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/Johann R. Richter/

Supervisory Patent Examiner, Art Unit 1616